10/798,317
Species

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
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NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
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NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
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NEWS	22	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	23	MAR 02	GBFULL: New full-text patent database on STN

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 18:08:31 ON 02 MAR 2005

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 18:08:41 ON 02 MAR 2005
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STRUCTURE FILE UPDATES: 1 MAR 2005 HIGHEST RN 840454-17-3
DICTIONARY FILE UPDATES: 1 MAR 2005 HIGHEST RN 840454-17-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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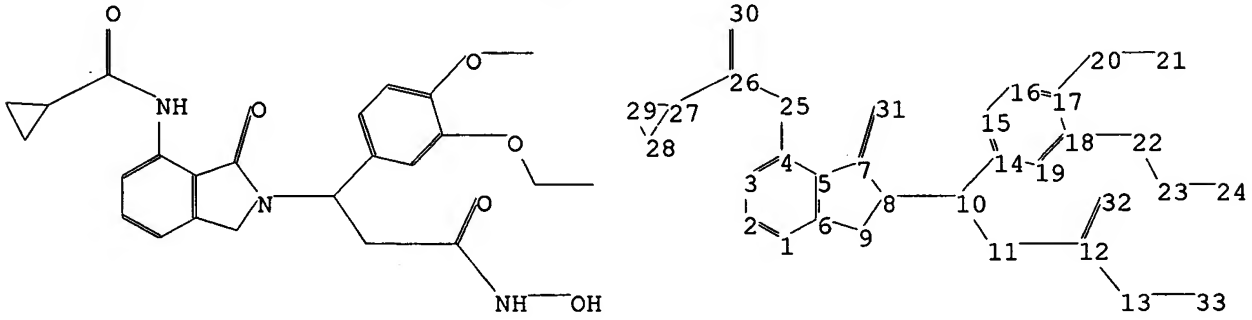

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ring bonds :

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exact/norm bonds :
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exact bonds :
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normalized bonds :
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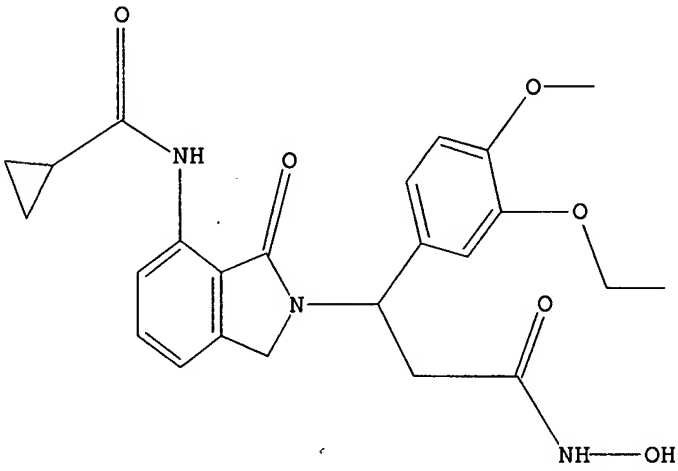


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Structure attributes must be viewed using STN Express query preparation.


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SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:             6 TO      266
PROJECTED ANSWERS:                0 TO        0

L2            0 SEA SSS SAM L1

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FULL SEARCH INITIATED 18:09:08 FILE 'REGISTRY'
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SEARCH TIME: 00.00.01

L3 3 SEA SSS FUL L1

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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FILE COVERS 1907 - 2 Mar 2005 VOL 142 ISS 10
FILE LAST UPDATED: 1 Mar 2005 (20050301/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L4 2 L3

=> d ibib abs hitstr tot

Instant app.

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:780510 CAPLUS
DOCUMENT NUMBER: 141:277486
TITLE: A preparation of 7-aminoisoindolone derivatives
INVENTOR(S): Man, Hon-Wah; Muller, George W.; Zhang, Weihong
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080423	A2	20040923	WO 2004-US7743	20040312
WO 2004080423	A3	20041104		
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004254214	A1	20041216	US 2004-798317	20040312
PRIORITY APPLN. INFO.:			US 2003-454155P	P 20030312
OTHER SOURCE(S):		MARPAT 141:277486		

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of 7-aminoisoindole derivs. of formula I [wherein: Y is C(O), CH2, CH2C(O), or SO2; X is H; Z is -alkyl-CO2H, alkyl, -alkyl-OH, or -alkyl-NH2, etc.; R1 and R2 are independently selected from (cyclo)alkyl or -alkyl-cycloalkyl], useful for treatment, prevention or management of cancer, inflammatory bowel disease, and myelodysplastic syndrome, etc. (no biol. data). For instance, isoindole derivative II was prepared via heterocyclization of aminopropanol derivative III and benzoic acid derivative IV with a yield of 64% (example 1).

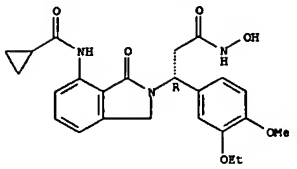
IT 760958-98-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)

RN 760958-98-1 CAPLUS

CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

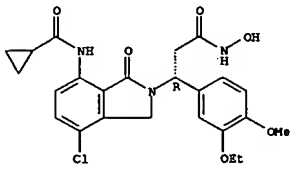


IT 760958-98-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)

RN 760958-98-3 CAPLUS

CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



same inventors

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:589381 CAPLUS
DOCUMENT NUMBER: 141:140314
TITLE: Preparation of 2-(fluoroalkoxyphenylalkyl)-1,3-dihydroisoindolones as PDE4, TNF-α, and/or MMP inhibitors
INVENTOR(S): Muller, George W.; Man, Hon-Wah; Zhang, Weihong
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060313	A2	20040722	WO 2003-US41568	20031229
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004204448	A1	20041014	US 2003-748085	20031229
PRIORITY APPLN. INFO.:			US 2002-436975P	P 20021230
OTHER SOURCE(S):		MARPAT 141:140314		

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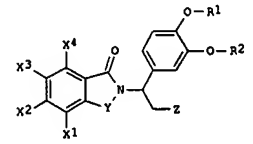

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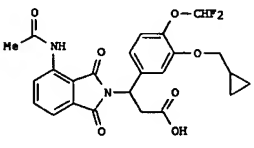


II

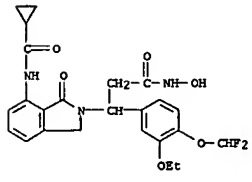
AB Title compds. I [wherein X1-X4 = independently H, halo, NO2, NH2, CF3,

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
alkyl, cycloalkyl(alkyl), NR7R8-(alkyl), R8CONH-(alkyl), NR7R8CONH-(alkyl), R8OCONH-(alkyl), R8O-(alkyl), imidazolyl(alkyl), pyrrolyl(alkyl), oxadiazolyl(alkyl), triazolyl(alkyl); or X1 and X2 or X2 and X3 or X3 and X4 may be taken together to form a (hetero)cycloalkyl ring; Y = CO, CH2, CH2CO, COCH2, SO2; Z = H, COR3, alkylsulfonyl(alkyl), alkyl, CH2OH, alkoxymethyl, CN; R1 and R2 = independently CHF2, alkyl, cycloalkyl(alkyl)]; at least one of R1 and R2 = CHF2; R3 = NR4R5, alkyl, OH, alkoxy, (un)substituted Ph, PhCH2; R4 and R5 = independently H, alkyl, OH, OCOR6; R6 = alkyl(amino), Ph, PhCH2, aryl; R7 and R8 = independently H, alkyl, cycloalkyl(alkyl), NR7R8-alkyl, R8O-alkyl, Ph, PhCH2, aryl; or pharmaceutically acceptable salts, hydrates, solvates, clathrates, stereoisomers, and prodrugs thereof] were prepd. For example, alkylation of 3,4-dihydroxybenzaldehyde with chlorodifluoromethane in the presence of K2CO3 in DMF gave 4-difluoromethoxy-3-hydroxybenzaldehyde (15%), which was further alkylated with bromomethylcyclopropane under the same conditions to afford 3-cyclopropylmethoxy-4-difluoromethoxybenzaldehyde (100%). Reaction of the benzaldehyde with ammonium acetate in 95% EtOH, followed by addn. of malonic acid provided 3-amino-3-(3-cyclopropylmethoxy-4-difluoromethoxyphenyl)propionic acid (52%). Condensation of the amine with 3-acetamidophthalic anhydride using sodium acetate in AcOH yielded the isoindoledione II (85%). I and their pharmaceutical compns., optionally in combination with another therapeutic agent, are useful for the treatment or prevention of diseases assocd. with phosphodiesterase 4 (PDE4) inhibition, abnormal tumor necrosis factor α (TNF-α) levels , and/or matrix metalloproteinase (MMP) inhibition, such as myelodysplastic syndrome, myeloproliferative disease, complex regional pain syndrome, cancer, inflammatory diseases, and autoimmune diseases (no data).

IT 725256-90-6P, Cyclopropanecarboxylic acid N-[2-[1-(4-difluoromethoxy-3-ethoxyphenyl)-2-hydroxycarbamoylethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PDE4, TNF-α, and/or MMP inhibitor; preparation of (fluoroalkoxyphenylalkyl)isoindolones as PDE4, TNF-α, and/or MMP inhibitors for treatment of inflammatory diseases, autoimmune diseases, cancer, and pain)

RN 725256-90-6 CAPLUS

CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)



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FULL ESTIMATED COST                                   10.33     171.87

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                   -1.46      -1.46

STN INTERNATIONAL LOGOFF AT 18:09:22 ON 02 MAR 2005
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10/798,317

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:sssptasel1626

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

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NEWS	2		"Ask CAS" for self-help around the clock
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NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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NEWS INTER	General Internet Information
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NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 18:09:41 ON 02 MAR 2005

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

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STRUCTURE FILE UPDATES: 1 MAR 2005 HIGHEST RN 840454-17-3
DICTIONARY FILE UPDATES: 1 MAR 2005 HIGHEST RN 840454-17-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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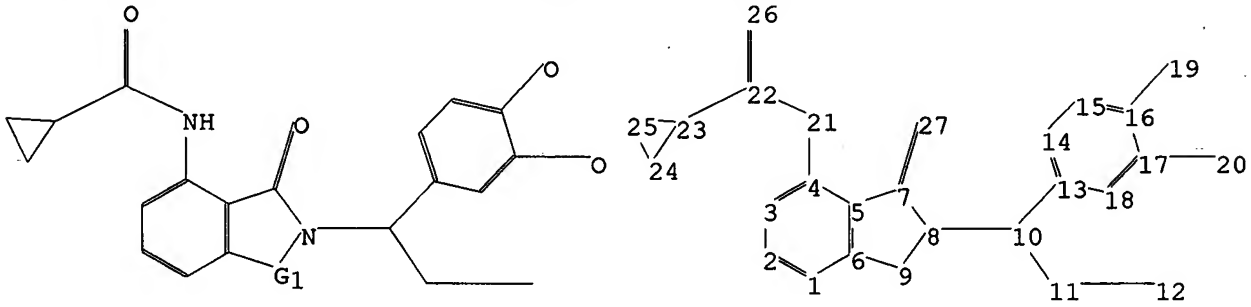

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ring nodes :
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chain bonds :
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ring bonds :
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exact/norm bonds :

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22-23 22-26 23-24 23-25 24-25
normalized bonds :
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G1:CH2,SO2,C,S

Match level :
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11:CLASS 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
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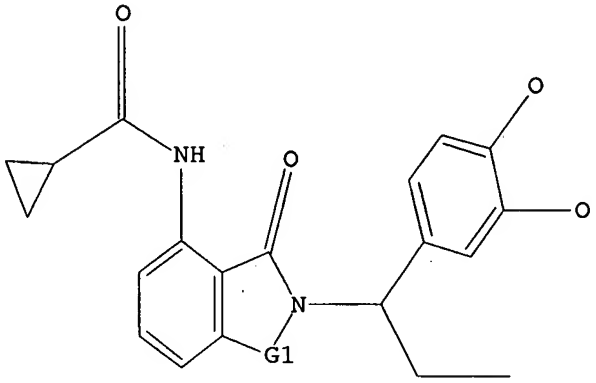


G1 CH2,SO2,C,S

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 18:10:09 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 11 TO ITERATE

100.0% PROCESSED 11 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 22 TO 418
PROJECTED ANSWERS: 2 TO 124

L2 2 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 18:10:12 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 222 TO ITERATE

100.0% PROCESSED 222 ITERATIONS 48 ANSWERS
SEARCH TIME: 00.00.01

L3 48 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	161.33	161.54

FILE 'CAPLUS' ENTERED AT 18:10:15 ON 02 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 2 Mar 2005 VOL 142 ISS 10
FILE LAST UPDATED: 1 Mar 2005 (20050301/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 5 L3

=> d ibib abs hitstr tot

Instant app

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:780510 CAPLUS
DOCUMENT NUMBER: 141:277486
TITLE: A preparation of 7-aminoisoindolone derivatives
INVENTOR(S): Man, Hon-Wah; Muller, George W.; Zhang, Weihong
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080423	A2	20040923	WO 2004-US7743	20040312
WO 2004080423	A3	20041104		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004254214	A1	20041216	US 2004-798317	20040312
PRIORITY APPLN. INFO.:			US 2003-454155P P	20030312
OTHER SOURCE(S):	MARPAT 141:277486			

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

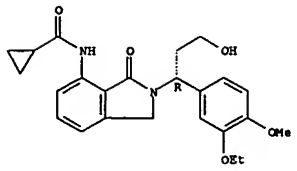
AB The invention relates to a preparation of 7-aminoisoindole derivs. of formula I
[wherein: Y is C(O), CH2, CH2C(O), or SO2; X is H; Z is -alkyl-CO2H, alkyl, -alkyl-OH, or -alkyl-NH2, etc.; R1 and R2 are independently selected from (cyclo)alkyl or -alkyl-cycloalkyl], useful for treatment, prevention or management of cancer, inflammatory bowel disease, and myelodysplastic syndrome, etc. (no biol. data). For instance, isoindole derivative II was prepared via heterocyclization of aminopropanol derivative III and
benzoic acid derivative IV with a yield of 64% (example 1).

IT **760958-78-9P 760958-80-3P 760958-88-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)

RN 760958-78-9 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-hydroxypropyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

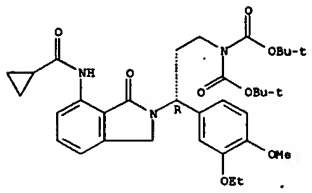
Absolute stereochemistry.

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



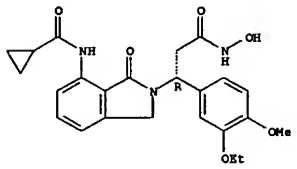
RN 760958-80-3 CAPLUS
CN Imidodicarbonic acid, [(3R)-3-[7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-2H-isoindol-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME).

Absolute stereochemistry.



RN 760958-88-1 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

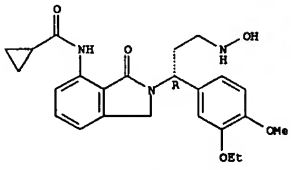


IT **760958-82-5P 760958-83-6P 760958-85-8P 760958-86-9P 760958-87-0P 760958-90-5P**

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
760958-91-6P 760958-93-8P 760958-96-1P
760958-97-2P 760958-98-3P 760958-99-4P
760959-04-4P 760959-06-6P 760959-09-9P
760959-12-4P 760959-13-5P 760959-14-6P
760959-15-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)

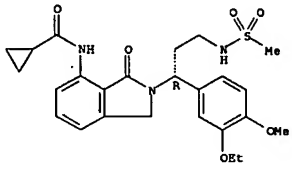
RN 760958-82-5 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 760958-83-6 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-[(methylsulfonyl)amino]propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

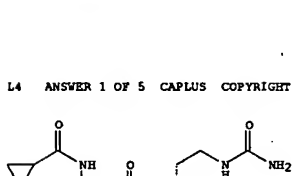
Absolute stereochemistry.



RN 760958-85-8 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-3-[(aminocarbonyl)amino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

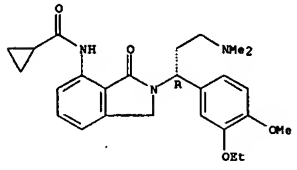
Absolute stereochemistry.

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 760958-86-9 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-3-(dimethylamino)-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

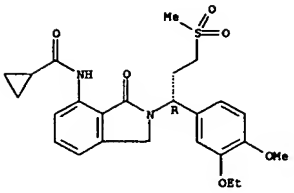


● HCl

RN 760958-87-0 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(methylsulfonyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

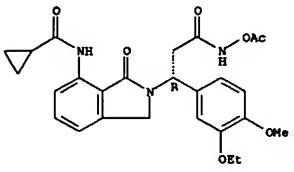
Absolute stereochemistry.

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



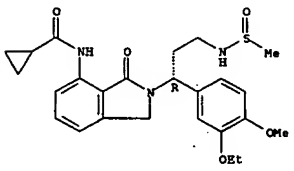
RN 760958-90-5 CAPLUS
CN 2H-Isoindole-2-propanamide, N-(acetyloxy)-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 760958-91-6 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-[(methylsulfinyl)amino]propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

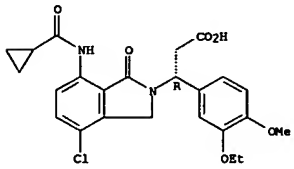
Absolute stereochemistry.



RN 760958-93-8 CAPLUS
CN 2H-Isoindole-2-propanoic acid, 4-chloro-7-[(cyclopropylcarbonyl)amino]-

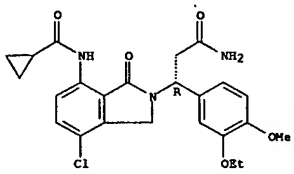
L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



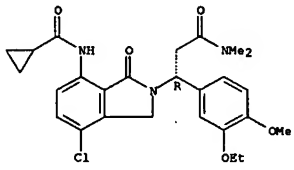
RN 760958-96-1 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 760958-97-2 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

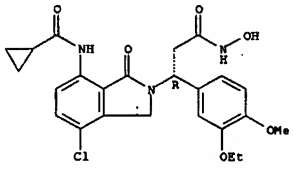
Absolute stereochemistry.



L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

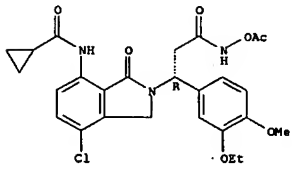
RN 760958-98-3 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

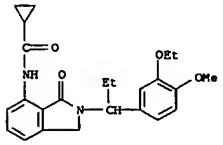


RN 760958-99-4 CAPLUS
CN 2H-Isoindole-2-propanamide, N-(acetyloxy)-4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

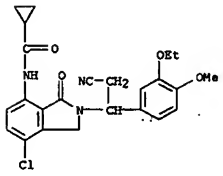


RN 760959-04-4 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



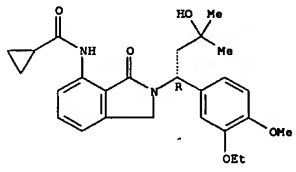
L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 760959-06-6 CAPLUS
CN Cyclopropanecarboxamide, N-[7-chloro-2-[2-cyano-1-(3-ethoxy-4-methoxyphenyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



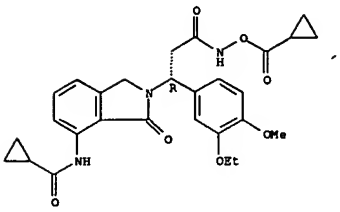
RN 760959-09-9 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-hydroxy-3-methylbutyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



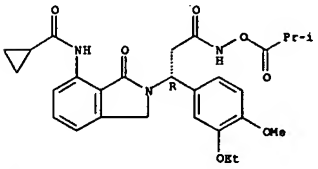
RN 760959-12-4 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-N-[(cyclopropylcarbonyl)oxy]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



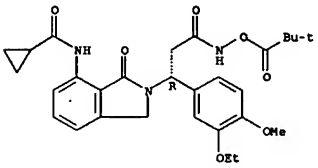
RN 760959-13-5 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-(2-methyl-1-oxopropoxy)-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

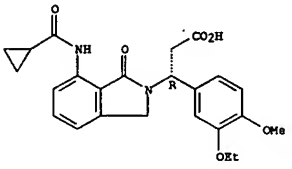


RN 760959-14-6 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-N-(2,2-dimethyl-1-oxopropoxy)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

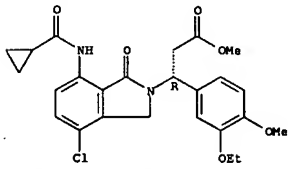


RN 760959-15-7 CAPLUS



RN 760958-94-9 CAPLUS
CN 2H-Isoindole-2-propanoic acid, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, methyl ester, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

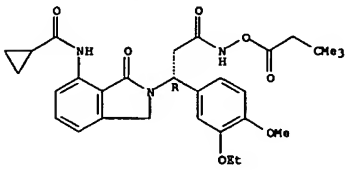


IT 760958-92-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)
RN 760958-92-7 CAPLUS
CN Ethanethioic acid, O-[(3R)-3-[7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-2H-isoindol-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

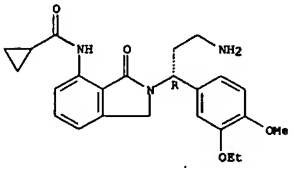
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-N-(3,3-dimethyl-1-oxobutoxy)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



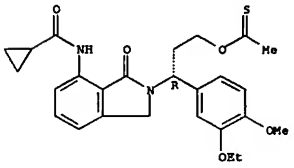
IT 760958-84-7 760958-89-2 760958-94-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)
RN 760958-84-7 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-3-amino-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 760958-89-2 CAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:780509 CAPLUS
DOCUMENT NUMBER: 141:295861
TITLE: A preparation of novel isoindolone derivatives, useful as PDE4 inhibitors
INVENTOR(S): Man, Hon-Wah; Muller, George W.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Same inventors

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080422	A2	20040923	WO 2004-US7742	20040312
WO 2004080422	A3	20041028		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004259873	A1	20041223	US 2004-798372	20040312
PRIORITY APPLN. INFO.:			US 2003-454149P P	20030312
OTHER SOURCE(S):			MARPAT 141:295861	

GI

notice of allowability - LS

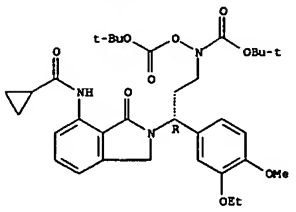
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of novel isoindolone derivs. of formula I [wherein: Y is C(O), CH2, CH2C(O), or SO2; R1 and R2 are independently selected from (cyclo)alkyl, CF2H, CF3, or CH2CHF2, etc.; Z1 is H, alkyl, NH2, or NH2, etc.; Z2 is H or CHO, -C(O)-alkyl, or -C(O)Ph, etc.; X1, X2, X3, and X4 are independently selected from H, halogen, NO2, CF3, alkyl, or alkylimidazolyl, etc.; R3 and R4 are independently H or alkyl], useful for treatment or prevention of various diseases and disorders, for example, diseases associated with PDE4 (no biol. data). For instance, isoindolone derivative II was prepared via amination of N-(hydroxypropyl)isoindolone derivative III by N,O-(tert-butoxycarbonyl)hydroxylamine with a yield of 78% (example 3).

IT **761434-16-6P 761434-20-2P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of novel isoindolone derivs., useful as PDE4 inhibitors)

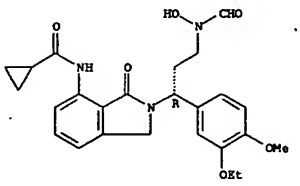
RN 761434-16-6 CAPLUS
CN Carbamic acid, [(3R)-3-[7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-2H-isoindol-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propyl][[(1,1-dimethylethoxy)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 761434-20-2 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(formylhydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

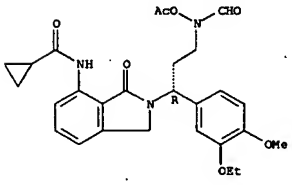


IT **761434-29-1P 761434-30-4P 761434-32-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel isoindolone derivs., useful as PDE4 inhibitors)

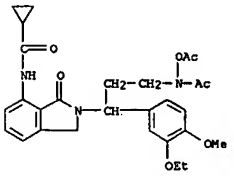
RN 761434-29-1 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-3-[(acetyloxy)formylamino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

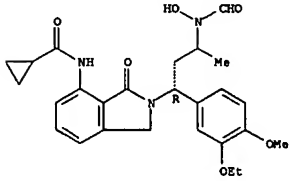


RN 761434-30-4 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[3-[acetyl(acetyloxy)amino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



RN 761434-32-6 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(formylhydroxyamino)butyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **761434-31-5**
RL: RCT (Reactant); RACT (Reactant or reagent)

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
NAME)

Absolute stereochemistry.

RN 761434-20-2 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(formylhydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

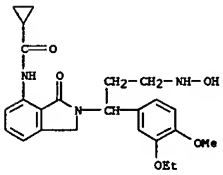
IT **761434-29-1P 761434-30-4P 761434-32-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel isoindolone derivs., useful as PDE4 inhibitors)

RN 761434-29-1 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-3-[(acetyloxy)formylamino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
(prepn. of novel isoindolone derivs., useful as PDE4 inhibitors)

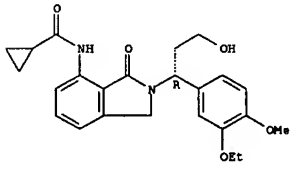
RN 761434-31-5 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



IT **760958-78-9P 760958-82-5P 761434-34-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel isoindolone derivs., useful as PDE4 inhibitors)

RN 760958-78-9 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-hydroxypropyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

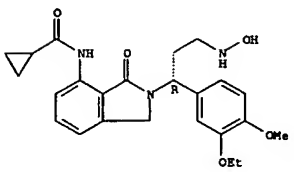
Absolute stereochemistry.



RN 760958-82-5 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

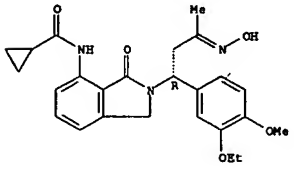
L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



same INV.

RN 761434-34-8 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyimino)butyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



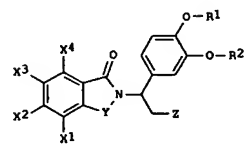
L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:589381 CAPLUS
DOCUMENT NUMBER: 141:140314
TITLE: Preparation of 2-(fluoroalkoxyphenylalkyl)-1,3-dihydroisoindolones as PDE4, TNF-α, and/or MMP inhibitors
INVENTOR(S): Muller, George W.; Man, Hon-Wah; Zhang, Weihong
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

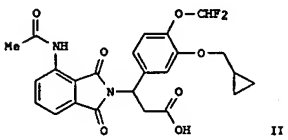
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060313	A2	20040722	WO 2003-US41568	20031229
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004204448	A1	20041014	US 2003-748085	20031229
PRIORITY APPLN. INFO.:			US 2002-436975P	P 20021230
OTHER SOURCE(S):	MARPAT 141:140314			

GI

method not applicable



I



II

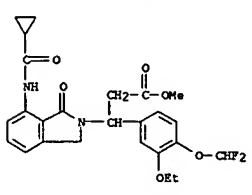
AB Title compds. I [wherein X1-X4 = independently H, halo, NO2, NH2, CF3,

L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

alkyl, cycloalkyl(alkyl), NR7R8-(alkyl), R8CONH-(alkyl), NR7R8CONH-(alkyl), R8OCONH-(alkyl), R8O-(alkyl), imidazolyl(alkyl), pyrrolyl(alkyl), oxadiazolyl(alkyl), triazolyl(alkyl); or X1 and X2 or X2 and X3 or X3 and X4 may be taken together to form a (hetero)cycloalkyl ring; Y = CO, CH2, CH2CO, COCH2, SO2; Z = H, COR3, alkylsulfonyl(alkyl), alkyl, CH2OH, alkoxymethyl, CN; R1 and R2 = independently CHF2, alkyl, cycloalkyl(alkyl); at least one of R1 and R2 = CHF2; R3 = NR4R5, alkyl, OH, alkoxy, (un)substituted Ph, PhCH2; R4 and R5 = independently H, alkyl, OH, OCOR6; R6 = alkyl(amino), Ph, PhCH2, aryl; R7 and R8 = independently H, alkyl, cycloalkyl(alkyl), NR7R8-alkyl, R8O-alkyl, Ph, PhCH2, aryl; or pharmaceutically acceptable salts, hydrates, solvates, clathrates, stereoisomers, and prodrugs thereof] were prepd. For example, alkylation of 3,4-dihydroxybenzaldehyde with chlorodifluoromethane in the presence of K2CO3 in DMF gave 4-difluoromethoxy-3-hydroxybenzaldehyde (15%), which was further alkylated with bromomethylcyclopropane under the same conditions to afford 3-cyclopropylmethoxy-4-difluoromethoxybenzaldehyde (100%). Reaction of the benzaldehyde with ammonium acetate in 95% EtOH, followed by addn. of malonic acid provided 3-amino-3-(3-cyclopropylmethoxy-4-difluoromethoxyphenyl)propionic acid (52%). Condensation of the amine with 3-acetamidophthalic anhydride using sodium acetate in AcOH yielded the isoindoledione II (85%). I and their pharmaceutical compns., optionally in combination with another therapeutic agent, are useful for the treatment or prevention of diseases assocd. with phosphodiesterase 4 (PDE4) inhibition, abnormal tumor necrosis factor α (TNF-α) levels , and/or matrix metalloproteinase (MMP) inhibition, such as myelodysplastic syndrome, myeloproliferative disease, complex regional pain syndrome, cancer, inflammatory diseases, and autoimmune diseases (no data).

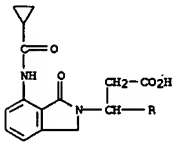
IT 725256-83-7P, 3-[7-(Cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid methyl ester 725256-87-1P, 3-[7-(Cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid 725257-12-5P, 3-[3,4-Bis(difluoromethoxy)phenyl]-3-[7-(cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]propionic acid RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(PDE4, TNF-α, and/or MMP inhibitor; preparation of (fluoroalkoxyphenylalkyl)isoindolones as PDE4, TNF-α, and/or MMP inhibitors for treatment of inflammatory diseases, autoimmune diseases, cancer, and pain)

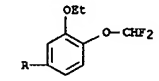
RN 725256-83-7 CAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



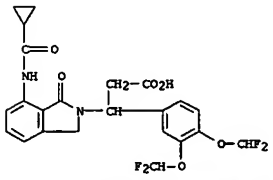
L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 725256-87-1 CAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)





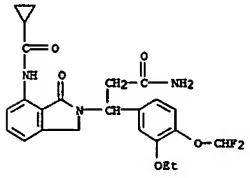
RN 725257-12-5 CAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



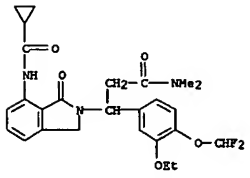
IT 725256-88-2P, Cyclopropanecarboxylic acid N-[2-[2-carbamoyl-1-(4-difluoromethoxy-3-ethoxyphenyl)ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide 725256-89-3P, Cyclopropanecarboxylic acid N-[2-[1-(4-difluoromethoxy-3-ethoxyphenyl)-2-(dimethylcarbamoyl)ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide 725256-90-6P, Cyclopropanecarboxylic acid N-[2-[1-(4-difluoromethoxy-3-ethoxyphenyl)-2-hydroxycarbamoylethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide 725257-02-3P, Cyclopropanecarboxylic acid N-[2-[2-carbamoyl-1-(4-difluoromethoxy-3-ethoxyphenyl)ethyl]-7-chloro-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide 725257-08-9P, 3-[3,4-Bis(difluoromethoxy)phenyl]-3-[4-chloro-7-(cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]propionic acid methyl ester 725257-11-4P , Cyclopropanecarboxylic acid N-[2-[1-[3,4-bis(difluoromethoxy)phenyl]-2-(dimethylcarbamoyl)ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide

725257-13-6P, Cyclopropanecarboxylic acid N-[2-[1-[3,4-bis(difluoromethoxy)phenyl]-2-carbamoylethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide 725257-14-7P, Cyclopropanecarboxylic acid N-[2-[1-[3,4-bis(difluoromethoxy)phenyl]-2-hydroxycarbamoylethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PDE4, TNF-α, and/or MMP inhibitor; prepn. of (fluoroalkoxyphenylalkyl)isoindolones as PDE4, TNF-α, and/or MMP inhibitors for treatment of inflammatory diseases, autoimmune diseases, cancer, and pain)

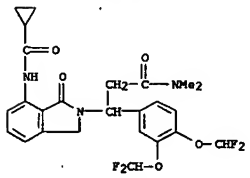
RN 725256-88-2 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



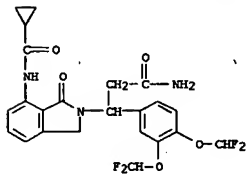
RN 725256-89-3 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)



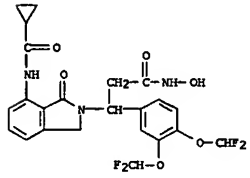
RN 725256-90-6 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)



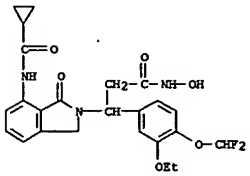
RN 725257-13-6 CAPLUS
CN 2H-Isoindole-2-propanamide, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



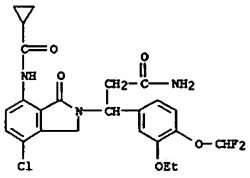
RN 725257-14-7 CAPLUS
CN 2H-Isoindole-2-propanamide, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)



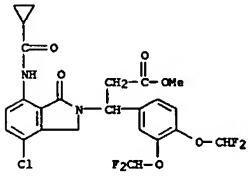
IT 725257-03-4, 3-[4-Chloro-7-(cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid 725257-15-8, 3-[3,4-Bis(difluoromethoxy)phenyl]-3-[7-(cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]propionic acid methyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)



RN 725257-02-3 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



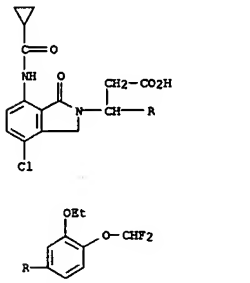
RN 725257-08-9 CAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3,4-bis(difluoromethoxy)phenyl]-4-chloro-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



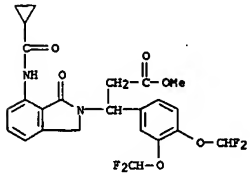
RN 725257-11-4 CAPLUS
CN 2H-Isoindole-2-propanamide, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)

(prepn. of (fluoroalkoxyphenylalkyl)isoindolones as PDE4, TNF-α, and/or MMP inhibitors for treatment of inflammatory diseases, autoimmune diseases, cancer, and pain)

RN 725257-03-4 CAPLUS
CN 2H-Isoindole-2-propanoic acid, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



RN 725257-15-8 CAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-, methyl ester (9CI). (CA INDEX NAME)



L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

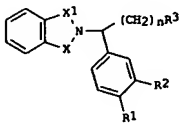
ACCESSION NUMBER: 2003:1001604 CAPLUS
DOCUMENT NUMBER: 140:42030
TITLE: Preparation of isoindolinediones as angiogenesis inhibitors.
INVENTOR(S): Man, Hon-wah; Muller, George W.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: U.S., 28 pp., Cont.-in-part of U.S. Ser. No. 590,344. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6667316	B1	20031223	US 2000-708199	20001108
CA 2392081	AA	20010517	CA 2000-2392081	20001109
WO 2001034606	A1	20010517	WO 2000-US30770	20001109
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1228071	A1	20020807	EP 2000-977095	20001109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 519459	A	20031128	NZ 2000-519459	20001109
JP 2004500346	T2	20040108	JP 2001-536553	20001109
NO 2002002223	A	20020708	NO 2002-2223	20020508
FI 2002000892	A	20020510	FI 2002-892	20020510
US 2004147588	A1	20040729	US 2003-685942	20031014

PRIORITY APPLN. INFO.:

US 1999-165168P	P	19991112
US 2000-590344	A2	20000608
US 2000-708199	A	20001108
WO 2000-US30770	W	20001109

OTHER SOURCE(S): MARPAT 140:42030
GI



I

AB Title compds. [I; R1, R2 = alkyl, alkoxy, cyano, cycloalkoxy, cycloalkyl, cycloalkylmethoxy; 1 of X and X1 = CO, SO2 and the other of X and X1 = CO, CH2, SO2, CH2CO; R3 = SO2Y, COZ, CN, hydroxyalkyl; Y = alkyl, Ph, PhCH2; Z = NR61R71, alkyl, Ph, PhCH2; R61 = H, alkyl, cycloalkyl, Ph, PhCH2, etc.; R71 = alkyl; 1 of R4, R5 = H and the other = imidazolyl, pyrrolyl,

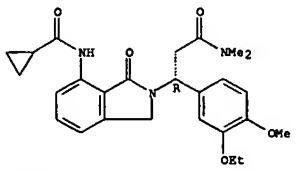
L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

oxadiazolyl, triazolyl, R6R7N(CzH2z); z = 0, 1; n = 1-3; R6 = cycloalkanoyl which is unsubstituted or substituted with halo, amino, monoalkylamino, dialkylamino; R4R5 = NHCH2R8, NHCOR8, N:CHR8; R7 = H, alkyl, methylsulfonyl, alkoxyalkylcarbonyl; R8 = CH2, O, NH, CH:CH, CH:N], were prepd. for treatment of undesirable angiogenesis (no data). Thus, 3,4-dinitrophthalic acid and 2-(3-ethoxy-4-methoxyphenyl)-1-(methylsulfonyl)eth-2-ylamine in PhMe were refluxed for 15 h through a Dean-Stark trap to give 49% 2-[1-(3-Ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4,5-dinitroisoindoline-1,3-dione. This was hydrogenated in EtOAc over Pd/C to give 73% 2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4,5-diaminoisoindoline-1,3-dione. The latter was refluxed 17 h with DMF di-Me acetal in HOAc to give 68% 7-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-3-pyrrolino[3,4-e]benzimidazole-6,8-dione.

IT 340019-72-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoindolinediones as angiogenesis inhibitors)

RN 340019-72-9 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:359998 CAPLUS
DOCUMENT NUMBER: 134:366799
TITLE: Preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases
INVENTOR(S): Man, Hon-Wah; Muller, George
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 94 pp. CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034606	A1	20010517	WO 2000-US30770	20001109
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6667316	B1	20031223	US 2000-708199	20001108
CA 2392081	AA	20010517	CA 2000-2392081	20001109
EP 1228071	A1	20020807	EP 2000-977095	20001109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 519459	A	20031128	NZ 2000-519459	20001109
JP 2004500346	T2	20040108	JP 2001-536553	20001109
NO 2002002223	A	20020708	NO 2002-2223	20020508
FI 2002000892	A	20020510	FI 2002-892	20020510

PRIORITY APPLN. INFO.:

US 1999-165168P	P	19991112
US 2000-590344	A	20000608
US 2000-708199	A	20001108
WO 2000-US30770	W	20001109

OTHER SOURCE(S): MARPAT 134:366799
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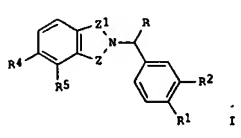


I

AB Title compds. [I; R = (CnH2n)R3; R1,R2 = (cyclo)alkyl(oxy), cyano, cycloalkylmethoxy; R3 = hydroxyalkyl, cyano, SO2R6, COR7; 1 of R4,R5 = H and the other = pyrrolyl, imidazolyl, (un)substituted amino(alkyl), etc.; R4,R5 = (un)substituted amino(alkyl); R4R5 = atoms to complete a ring; R6 = alkyl, Ph, CH2Ph; R7 = groups cited for R6, (un)substituted amino; 1 of Z,Z1 = CO or SO2 and the other = CH2, CO, SO2, CH2CO; n = 1-3] were prepared for treatment of phosphodiesterase- and TNFα-mediated diseases (no

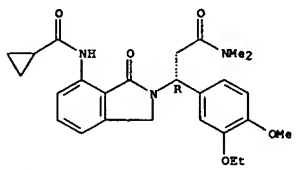
L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

data). Thus, 3,4-dinitrophthalic acid was cyclocondensed with H2NCH(CH2SO2Me)CGH3(OEt)(OMe)-3,4 and the product reduced to give I (R = CH2SO2Me, R1 = OMe, R2 = OEt, R4 = R5 = NH2, Z = Z1 = CO).

IT 340019-72-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)

RN 340019-72-9 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	25.15	186.69

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.65	-3.65

STN INTERNATIONAL LOGOFF AT 18:10:27 ON 02 MAR 2005